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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,946	JOMAA, HASSAN	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-20 and 52-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-20 and 52-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions Acknowledged

1. Applicant's request for withdrawal of the election requirement between Group (i) and Group (ii) in addition to the secondary election requirement deems to be persuasive. Acknowledgement is made of applicant's contention that the autoantigens encompassed by Group (i) and the allergens of Group (ii) are functional equivalents that are recognized in the art as capable of triggering immune system responses in sensitive or affected individuals. Therefore, the examiner withdraws the election requirement mailed June 29, 2004.

Status of Application

2. The request filed on January 07, 2004 for a Request for Continued Examination (RCE) under 37 CFR 1.114 is accepted and a RCE has been established. An action on the RCE follows.

3. Claims 15-20 and 52-65 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 15-20, 54-56, 58-59 and 62-65 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for a medicament for treating the specific autoimmune disease, for example rheumatoid arthritis, with the specific bisphosphonic acid (e.g., 3-amino-1-hydroxypropylidene-1,1-bisphosphonate) in combination with the specific autoantigen (e.g., collagen II antigen), does not reasonably provide enablement for the term

"treating an autoimmune disease" with the medicament comprising compounds of formula (I) in combination with the autoantigens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

All rejected claims are drawn to the methods of treating autoimmune disease in patients with the administration of the instant medicament. The nature of the invention is extremely complex in that it encompasses anticipating multiple complex disorders (more than 80 serious disorders) having unrelated manifestations and subsequently administering the numerous possible combinations of the instant medicaments.

(2) The state of the prior art

There are no known compounds of similar structure or combination product which have been demonstrated to treat all types of autoimmune diseases.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. Applicant has not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for accomplishing the desired result of the claimed invention without undue amount of experimentation. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970).

(5) The breadth of the claims

The claims are very broad. The breadth of the claims encompasses multiple sclerosis, rheumatoid arthritis, hashimoto thyroiditis, myasthenia gravis, lupus erythematosus, diabetes mellitus, primary biliary cirrhosis, hepatis, adrenalitis/Addison's disease, polymyositis, dermatomyositis, autoimmune haemolytic anaemia, myocarditis, myopericarditis, scleroderma, uveitis, pemphigus vulgaris, pemphigoid, pernicious anaemia, Crohn's disease, ulcerative colitis, etc...

Furthermore, the breadth of the instant claims is complicated by numerous possible combinations of the bisphosphonic acid derivatives of the formula I and autoantigens (e.g., nervous system tissue extracts, collagen, thyroglobulin, acetylcholine receptor protein, DNA, islet cell extracts, human insulin, liver extracts, adrenal cortex extracts, skin extracts, etc...).

(6) The amount of direction or guidance presented or (7) The presence or absence of working examples

The specification discloses that the reinduction of tolerance achieved with oral or inhalatory administration of autoantigens or allergens specific to the disorder is greatly promoted if the autoantigens or allergens is administered in combination with bisphosphonic acids or the derivatives thereof (page 3, lines 13-21). To support the claimed invention, the inventor is relied on the prior art knowledge in the use of bisphosphonic acids and of some of the derivatives thereof in pharmaceutical preparations (page 3, lines 23-25) and the immunomodulatory activity of bisphosphonic acids (page 3, lines 32-34).

As examples of suitable bisphosphonic acid for the instant invention, compounds of the general formula (I) are disclosed, specifically, "aminohydroxymethylidenebisphosphonic acid (AMP), 2-amino-1-hydroxyethylidene-1,1-bisphosphonic acid (AEP)..." (page 9, line 10 thru page 10, line 2). Furthermore, various autoantigens (e.g., collagen, thyroglobulin, acetylcholine receptor protein, islet cell extracts, liver extracts, etc...) are disclosed in the specification (page 10, line 10 thru page 11, line 14).

However, there is no demonstrated correlation that the tests and results apply to all of the disorders or disease conditions embraced by the instant claims. The specification fails to provide sufficient information allowing the skilled artisan to envision the desired result of the claimed invention without undue amount of experimentation.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides

a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue amount of experimentation to ascertain "treating an autoimmune disease that would enabled in this specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 15-17, 20 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Yates (US 5646134).

Yates teaches an implant composition containing alendronate in a collagen/mineral mixture (column 3, line 60 thru column 4, line 9).

Although Yates is silent about properties or characteristics of "treating an autoimmune disease" and/or "autoantigen specific for the autoimmune disease", such property or characteristic is deemed to be inherent to the composition, i.e., it was always there. It is noted to applicant that claims to a composition possessing a particular property or characteristic are still properly rejected by a reference to the same composition, even if the reference does not address or acknowledge the property.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 15-20 and 52-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyons et al. (GB 2312165 A) in view of Michael et al. (US 6174529 B1) and Daifotis et al. (WO 96/39151), and if necessary further in view of applicant's admission of the prior art (see Applicant's Response to the Election Requirement, Remarks filed July 28, 2004, page 14).

Claims read on a medicament comprising bisphosphonic acids represented by general formula (I) and an autoantigen or allergen.

Lyons (GB 2312165 A) teaches or suggests the use of bisphosphonic acids (e.g., ibandronate) for treating chronic immune system activation disorders by an immunomodulaotry action (claim 1, 3, 11 and page 1, lines 5-7).

Daifotis teaches the use of bisphosphonic acid derivatives such as alendronate, etidronate, pamidronate, clodronate, risedronate and tiludronate as the functional equivalents of ibandronate (page 2, lines 6-18).

Michael teaches or suggests the use of antigens (e.g., insulin, thyroid proteins, acetyl choline receptor protein, Type II collagen, myelin basic protein) or allergens (e.g., dust, mites, bee venom, food allergens, animal dander, insect venoms, etc...) as "therapeutic protein (column 1, lines 18-45; column 2, lines 59-67; column 3, lines 33-50) for treating autoimmune diseases or allergies.

The teaching Lyons differs from the claimed invention in the combination use of the specific bisphosphonic acid of the formula I in combination with autoantigens or allergens. To incorporate such teaching into the teaching of Lyons, would have been obvious in view of Micahel who teaches or suggests the use of protein antigens (e.g., insulin, thyroid proteins, acetyl choline receptor protein, Type II collagen, myelin basic protein) or allergens (e.g., dust, mites, bee venom, food allergens, animal dander, insect venoms, etc...) as "therapeutic protein (column 1, lines 18-45; column 2, lines 59-67; column 3, lines 33-50) for treating autoimmune diseases or allergies and Daifotis who teaches the use of bisphosphonic acid derivatives such as alendronate, etidronate, pamidronate, clodronate, risedronate and tiludronate as the functional equivalents of ibandronate.

Above references in combination make clear that bisphosphonic acids and protein antigens or allergens have been individually used for the treatment of autoimmune diseases. It is obvious to combine two compositions each of which is taught by prior art to be useful for same

purpose; idea of combining them flows logically from their having been individually taught in the prior art.

With respect to the selection of the specific species of the formula I or the specific species of the secondary ingredients, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to select any of the species of the formula I (i.e., alendronate, etidronate, pamidronate, clodronate, risedronate and tiludronate) or any of the secondary ingredients because an ordinary artisan would have the reasonable expectation that any of the species of the genus or any of the species of the autoantigens or allergens would have similar properties or recognized functional equivalents in the art, and thus, the same use as the genus as a whole.

Conclusion

6. No Claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

VICKIE KIM
PRIMARY EXAMINER

Brian Kwon
Patent Examiner
AU 1614